opportunity of changing the cell chemistry so that they may penetrate the cell. When applied to these cells in a manner which prevents their rapid removal the cells may undergo a change which permits of their penetration. Any procedure which increases metabolic activity of cells ensures a greater degree of *intra vitam* staining with trypan blue. Whether such an increase, with its attending cell injury as would result from the introduction subdurally of relatively large doses of the stain, or, analogously speaking, large doses of salvarsan are harmless and beneficial, cannot be stated.

It would seem proper to conclude that when dealing with colloidal stains or drugs the meninges are more accessible by subdural than by intravenous routes. This cannot be stated of the central nervous system. When intravenously introduced, certain dyes and salvarsan fail to reach the central nervous system largely because of the physicochemical reactions between the substance and the tissues. The permeability of the bloodvessels plays but a small role and the cerebrospinal fluid and choroid plexus none at all.

Finally, salvarsan, which probably like trypan blue leaks from bloodvessels relatively slowly, when intravenously introduced possesses as great a spirochetocidal action upon those organisms situated in the pia, adventitia and perivascular lesions in the brain as elsewhere, providing the spirochetes have not developed a peculiar resistance to such a drug.

THE CIRCULATORY REACTIONS TO GRADUATED WORK IN NORMAL PEOPLE AND IN THOSE WITH CARDIAC INSUFFICIENCY.

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NEW YORK.

(From the Second Medical Division of the New York Hospital.)

The important part which physical training plays in the preparation of soldiers for active service and in promoting convalescence from disease or injury makes it desirable to reinvestigate the circulatory reactions following work in both normal people and in those with damaged hearts to see if we can find in these reactions anything which will serve as a guide in estimating the condition of the cardiac reserve power.

We shall first take up the effects of work upon the systolic blood-pressure in normal people. There are two methods of determining the pressure curve after work. In one described by Rapport,[1] readings are taken very frequently (five- to ten-second intervals) by

[1] Arch. Int. Med., 1917, xix, 981.

palpation. In the other method, whieh we have used for some time, readings are made less frequently by auscultation and at practically equal intervals. Our method is mueh more convenient, and enables us, as we will shortly show, to construct the curve with sufficient aecuracy to achieve our purpose.

For these experiments a sphygmomanometer of the Riva-Rocci type, with n web-covered rubber bulb, was used. The pressure was read by auscultation until it had reached a constant level. The cuff remained on the arm during work and a reservoir of air under pressure was maintained in the rubber bulb. With coöperation on the part of pntient and assistant we were generally able to make the first reading, when so desired, as soon as ten seconds had elapsed, nnd at short intervnls thereafter. When using our own method[2] of infrequent readings we made the first reading between twenty-five and thirty seconds after work; the second between fifty-five and sixty; the third between eighty-five and ninety. We endeavored to make the readings as elose to thirty, sixty and ninety seconds as was possible.

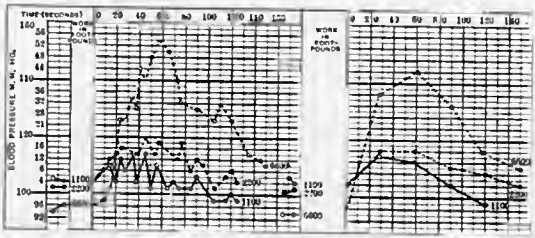

CHART I.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the iodividual exercises. In this and in the succeeding charts the curves oo the left were plotted by the frequent method of measuremeot aod oo the right by the infrequent method.

We have seleeted Charts I nnd II from a number of others as exemplifying the usual reaetions following incrensing amounts of work in a normal man. The blood-pressure eurves nre plotted both by the method of frequent reading and by our own method of reading at stated intervals.

The systolie blood-pressure shortly (ten to fifteen seconds) after small or moderate amounts of work is raised; it then mounts rapidly, attaining its summit generally inside of forty seconds and rapidly

[2] In our earlier work the first measuremeots of the blood-pressure were made betweeo tweoty and thirty secoods after work, the secood measuremeot between fifty aod sixty seconds after aod the third measuremeots nioety secoods after. The method described io this article uodoubtedly gives a more accurate represeotation of the blood-pressure curve.

subsides. The height of the first readings and of the subsequent rise is dependent, as a rule, on the amount of work and the time in which it is performed.

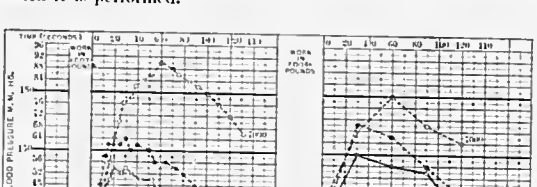

Chart II.—Blood-pressure reactions in a normal man after increasing amounts of work furnished by swinging dumb-bells. Five to ten minutes intervened between the individual exercises.

Following the greatest amounts of work the rise is delayed so that the summit is reached after fifty or more seconds and the subsidence to normal is gradual instead of rapid. This last extreme reaction is what we have termed in our earlier articles a "delayed rise." Cotton, Rapport and Lewis[3] prefer to call this a "delayed summit." The results stated above agree quite closely with their conclusions.

The time at which the pressure reaches its maximum is of considerable importance because it indicates either a rapid or slow development of the blood-pressure curve. In a normal person in good physical training the summit is reached, after all but the heaviest amounts of work, before fifty seconds have elapsed. When the work reaches the limit of effort, judging from the performer's sensations and degree of breathlessness, there ensues a delayed rise, the summit of the pressure falling somewhere between fifty and ninety seconds, and the curve then slowly subsides to normal.

The term "delayed rise" will be used, therefore, to indicate that form of the systolic blood-pressure curve which shows a delayed rise, with a summit occurring between fifty and ninety seconds after work. It presents no qualitative difference from the curves following moderate amounts of work, but is simply an exaggeration of what might be called the "normal type." An examination of the curves obtained by the infrequent method of measurement (see Chart I) shows that a delayed rise, with all that it implies as to the form of the pressure curve, will be revealed by this much simpler method with almost as much certainty as by Rapport's method.

This circulatory reaction possesses, we believe, peculiar significance, and we will enumerate the facts we have discovered about the delayed rise following work in normal people.

[3] Heart, 1917, vi, 269.

The Delayed Rise in Normal People. (*a*) In a normal person in good physical training a delayed rise is found only after heavy work, and is accompanied by marked breathlessness. The limit of effort is apparently approached when this reaction ensues.

The amounts of work which delay the summit to between fifty and ninety seconds vary for different persons according to their condition of physical training.

We have never failed to elicit a delayed rise in normal people at some stage as they performed progressively increasing quantities of work.

(*b*) A normal person in poor physical training will show a delayed rise after moderate amounts of work which are not accompanied by as marked breathlessness as is noted under (*a*).

(*c*) The production of a delayed rise is dependent on the amount of work and the time in which it is performed (power expended) and not on the group of muscles employed.[4]

(*d*) The amount of work which is followed by a delayed rise varies but little from day to day. Chart III exemplifies this.

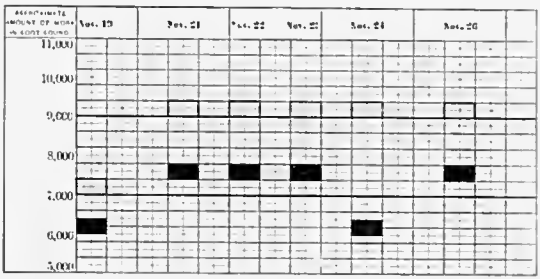

CHART III.—Daily variations in amounts of work performed by normal persons which were followed by delayed rises. The black squares represent work which was not followed by a delayed rise. Shaded squares represent work which was followed by a delayed rise.

(*e*) Children are able to perform relatively larger amounts of work without producing a delayed rise than are adults, taking into consideration their respective weights.[5] After thirty years of age the amounts of work which can be performed without evoking delayed rises gradually decrease.

(*f*) Physical training increases rapidly the amounts of work which can be performed without delayed rises ensuing.

[4] Arch. Int. Med., 1916, xvii, 366. Although not so stated, all first measurements in this article were made between twenty and thirty seconds after work.

[5] Personal communication, Dr. W. P. St. Lawrence.

(*g*) During convalescence from infectious diseases the amounts of work which can be performed without delayed rises are small at first and then increase rapidly.[6]

The Systolic Blood-pressure after Work in Patients Suffering from Marked Cardiac Insufficiency. Two patients with rhythmical pulses were selected whose cardiac reserve powers were obviously exhausted and their curves after work were plotted by both the frequent and the infrequent methods of reading the blood-pressure.

The first patient, M. W., aged twenty-one years, was suffering from an old rheumatic endocarditis which had left him with a double mitral and an aortic lesion. As he lay in bed he was dyspneic, his legs were swollen, the liver was enlarged and there were many moist rales at the base of the lungs.

CHART IV.—Blood-pressure reactions after increasing amounts of work furnished by flexing dumb-bells in patient M. W., suffering from extreme cardiac insufficiency (reserve power = 0).

The second patient, L. G., aged seventeen years, was suffering from cardiac insufficiency following a rheumatic lesion of the mitral and aortic valves. He was dyspneic as he sat in a chair, both lungs showed moist rales at the bases and his liver was enlarged. He had no pretibial edema. Chart V shows his blood-pressure reactions.

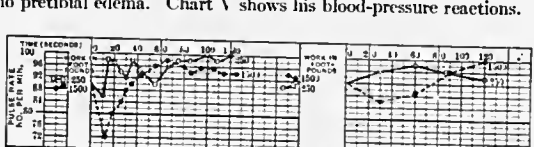

CHART V.—Blood-pressure reactions after increasing amounts of work furnished by dumb-bell movements in patient L. G., suffering from marked cardiac insufficiency (reserve power = 0).

The blood-pressure curves in these charts are quite typical of the curves we have obtained in all patients suffering from grave cardiac insufficiency. The first reading is often below that noted before work. As the work is increased the first reading frequently falls lower and lower. This peculiarity is also often observed when we use the infrequent method of plotting the curve. The development of the curve is greatly prolonged, as is evidenced by the marked delay

[6] Personal communication, Dr. Hubert Mann.

in the rise. The amounts of work which produce this curve are very small as compared with those in normal subjects. Chart V shows very well the effect of a marked increase in work. Instead of mounting higher, as it would in a normal person, the initial drop of the blood-pressure was simply accentuated. The curve otherwise greatly resembles that following the much smaller amount of work.

The similarity between these curves, obtained in patients with no cardiac reserve power, and the curves with a delayed rise in normal people, is marked and affords a valuable clue to the significance of this type of blood-pressure curve.

The Systolic Blood-pressure after Work in Patients Suffering from Moderate Cardiac Insufficiency. The patient whose curves are represented in Chart VI was selected as a typical example of this class of patients. She was an ambulatory patient with mitral stenosis arising from rheumatic endocarditis. She was able to walk on the level slowly without discomfort. Going up one flight of stairs (twenty steps) caused marked breathlessness and palpitation, obliging her to stop and rest after ten steps. She had no edema of the legs or lungs.

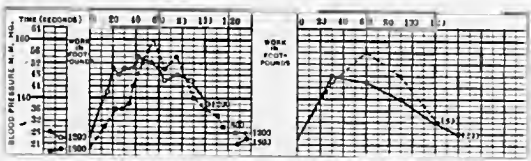

CHART VI.—Blood-pressure reactions in a patient with moderate cardiac insufficiency after increasing amounts of work furnished by dumb-bell movements. Five to ten minutes intervened between the individual exercises.

It will be noted that 1800 foot-pounds of work was followed by a delayed rise and was accompanied by marked dyspnea and palpitation. She was able to perform 1200 foot-pounds without causing a delayed rise and with but moderate breathlessness.

Improvement in Cardiac Insufficiency and its Effect upon the Delayed Rise. Patients suffering from varying degrees of cardiac insufficiency show, as they improve, a steady increase in the amounts of work they are able to perform without causing this reaction. Chart VII exemplifies the foregoing statement.

The Significance of the Delayed Rise in Systolic Blood-pressure. The primary meaning of this reaction is that the curve of the systolic blood-pressure, if plotted out, would have the form described and depicted in the first part of this article.

In order to appreciate the significance of this form of the blood-pressure curve the facts we have enumerated about this reaction in normal people must be considered. Of these the most important

are the invariability of the delayed rise after a stated amount of work performed in a stated time quite irrespective of the group of muscles

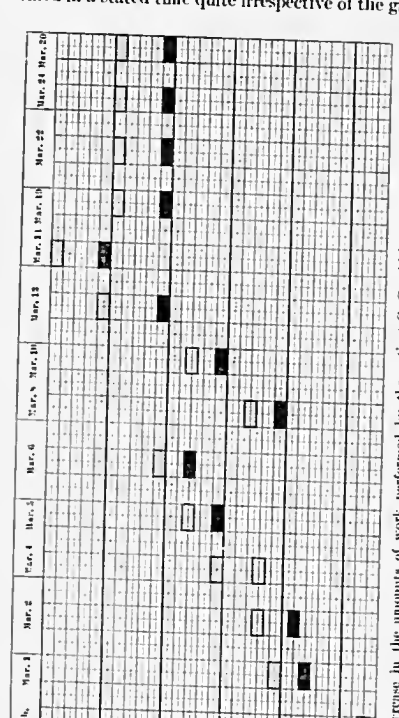

CHART VII.—The increase in the amounts of work performed by the patient *G. C.* which were not followed by delayed rises. This patient at the outset suffered for one month from extreme cardiac insufficiency, and, coincident with the work increase, his clinical condition improved markedly. The black squares represent work which was not followed by a delayed rise; the shaded squares, work which was. The empty squares indicate that any work whatsoever was followed by a blood-pressure curve similar to those in Charts IV and V.

employed; the small variations from day to day of the quantities of work which cause this reaction; the relatively greater amounts of

work which children, as compared to adults, can perform, taking their respective weights into consideration, before this reaction ensues; and the marked effect which physical training has in increasing the amounts of work a person can accomplish without evoking a delayed rise.

It is the type of curve obtained after minimal amounts of work in patients with no cardiac reserve power, however, which does most to make clear the meaning of this reaction in healthy people. These curves always show a delayed rise with a very slow return to normal, and are quite similar to the curves initiated by a delayed rise in normal persons.

TABLE I.—PULSE REACTIONS IN NORMAL MEN.

Patient.	Work.	Pulse rate		Return to normal, seconds	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J. M., aged twenty-four years.	20 S. 5	96	112	120	No	
	20 S. 10	72	118	180	No	
	30 S. 10	80	120	180	Yes	58
	20 S. 20	88	128	240	Yes	60
	20 S. 30	88	140	300	Yes	60
A. Q., aged twenty-six years.	15 S. 10	72	101	120	No	
	15 S. 15	72	108	118	Yes	60
	15 S. 20	70	101	120	No	
	20 S. 20	88	128	120	Yes	60
	30 S. 20	68	121	300	Yes	60
	30 S. 20	68	112	120	No	
	30 S. 25	72	128	120	No	
	30 S. 30	81	112	180	Yes	60
	30 S. 20	81	112	180	No	
	30 S. 25	88	136	120	Yes	60
	30 S. 35	88	136	240	Yes	60
R. O., aged twenty-three years.	20 S. 10	101	128	120	No	
	20 S. 15	101	140	180	No	
	20 S. 25	101	158	180	Yes	60
	20 S. 35	101	156	240	Yes	60
W. M., aged twenty-two years.	20 S. 15	90	112	180	No	
	20 S. 20	96	128	120	Yes	60
	20 S. 25	96	121	120	Yes	60
R. T., aged forty-one years.	20 S. 30	88	120	150	No	
	20 S. 35	84	136	210	No	
	20 S. 40	84	140	300	No	
	20 S. 45	84	118	360	Yes	60

The effect of work upon the pulse rate of normal men. There was a period of from five to ten minutes between the individual exercises. The figures 120 in the column headed "Return to Normal" means that the rate became normal after two minutes *or earlier*.

Another fact which has an important bearing on this question is that, coincident with the improvement of patients suffering from cardiac insufficiency, there occurs an increase in the amounts of work they can perform without producing delayed rises.

There is but one conclusion, it seems to us, which can be drawn

from these facts, and that is that a delayed rise of systolic blood-pressure, with all that it implies as to the form of the pressure curve, means that the preceding work has either overtaxed or is on the point of overtaxing the heart's reserve power. If this conclusion is correct it is a simple matter to use comparisons of the amounts of work causing the delayed rise as an indirect measure of the cardiac reserve power.

TABLE II.—PULSE REACTIONS IN PATIENTS WITH CARDIAC INSUFFICIENCY.

Patient.	Work in foot pounds.	Pulse rate.		Return to normal, seconds.	Delayed rise, systolic pressure.	Delay, seconds.
		Before.	Immediately after.			
J.S., aged twenty-seven years. Marked cardiac insufficiency. Reserve power zero.	200	100	116	180	Yes	90
	200	116	124	120	Yes	120
	300	112	120	120	Yes	120
	300	120	128	120	Yes	88
M. W., aged twenty-seven years. Marked cardiac insufficiency. Reserve power zero.	60	104	108	120	Yes	60
	140	108	110	180	Yes	90
	280	112	112	120	No	
	400	112	116	120	Yes	120
	400	106	112	120	Yes	88
	456	112	120	180	Yes	120
	140	108	110	125	Yes	90
	280	106	118	120	Yes	85
	600	112	118	120	Yes	60
	146	108	116	120	No	
	200	108	114	120	Yes	58
	200	108	118	120	Yes	90
L. G., aged seventeen years. Moderate insufficiency.	600	84	104	120	Yes	90
	1200	88	112	120	Yes	90
	250	66	80	120	No	
	375	64	76	120	Yes	90
	500	64	80	120	Yes	90
	750	68	88	120	Yes	58
	1200	76	108	120	Yes	88
	250	84	88	120	Yes	60
	500	72	80	120	Yes	60
	750	76	104	180	Yes	60
	200	72	100	120	No	
	500	76	100	180	No	
	750	80	100	120	Yes	90
	1200	78	118	118	Yes	88
	2000	78	132	240	Yes	90
	250	90	102	120	Yes	60
	900	90	112	300	Yes	118
	1400	92	128	180	Yes	120
S. T., aged fifty-eight years. Moderate cardiac insufficiency.	700	76	88	120	No	
	2000	74	96	120	Yes	90
E. C., aged thirty-four years. Moderate cardine insufficiency.	170	92	108	120	No	
	340	88	80	...	No	
	1100	84	104	120	No	
	2000	80	...	180	Yes	60

The effect of work upon the pulse rate of patients suffering from varying degrees of cardiac insufficiency. Five to ten minutes intervened between the individual exercises. The figure 120 in the column headed "Return to Normal" means that the rate became normal after two minutes *or earlier*.

The Effect of Work upon the Pulse Rate in Normal Individuals. It has been our experience that changes in pulse rate following work have seldom afforded any reliable indication as to the condition of the heart's reserve power. Recently, Mekins and Gunson[7] have published their investigations upon the effect of exercise on the pulse rate in patients suffering from "disordered action of the heart." One of their conclusions was that patients in whom the pulse rate did not return to normal within a short period of time (*i. e.*, two minutes) performed the simplest exercises with difficulty. With this particular conclusion in mind we have observed the pulse rate after work in a few normal people and in a few patients with cardiac insufficiency.

The pulse was counted before exercise and then for fifteen seconds immediately after exercise. At the end of one hundred and ten seconds it was then counted again for twenty seconds. From these counts the rates per minute immediately after work and at the end of one hundred and twenty seconds were calculated. If the rate at the end of two minutes was within six beats of the pre-exercise rate it was considered to have returned to normal. Table I summarizes our results in normal people.

There were 27 experiments carried out on five normal men. A delayed rise of the systolic pressure occurred fourteen times and was accompanied nine times by a pulse rate which did not return to normal inside of two minutes. Thirteen times there was no delayed rise, and yet on seven occasions the pulse rate did not return to normal inside of two minutes.

The Effect of Work upon the Pulse Rates of Patients Suffering from Varying Degrees of Cardiac Insufficiency. Table II summarizes our results in patients who had either a moderate or no cardiac reserve power.

There were 40 experiments carried out on 5 patients. A delayed rise of the systolic pressure occurred 31 times and was accompanied 9 times by a pulse rate which did not return to normal inside of two minutes. Twenty-two times the pulse rate returned to normal two minutes or sooner after work.

The results of these experiments, carried out on normal persons and those suffering from cardiac insufficiency, few in number though they are, tend to confirm our belief that the time required for the pulse rate to return to normal affords but little information, in either normal people or patients with cardiac insufficiency, as to the condition of the heart's reserve power.

Conclusions. The occurrence of a delayed rise in systolic blood-pressure after work indicates that the preceding work has either overtaxed or is on the point of overtaking the heart's reserve power. The presence of a delayed rise can be determined by the

[7] Heart, 1917, vi, 285.

infrequent method of plotting the pressure curve with almost as much certainty as by the frequent method.

A small number of experiments upon normal people and upon patients with cardiac insufficiency showed that no definite relation existed between the time required for the pulse rate to return to normal and the condition of the cardiac reserve power.

We wish to express our thanks to Dr. William R. Williams, whose hospital service furnished the material for the foregoing work, for his advice and coöperation in carrying out the same.

PERFORATED GASTRIC AND DUODENAL ULCER: A STATISTICAL REPORT OF FIFTY-NINE CASES.

By Francis J. Scully, M.D.,

Research Fellow, Cook County Hospital, Chicago.

(From the Clinics of the Cook County Hospital.)

During the last six years (1911 to 1916 inclusive) there were 59 cases of perforated gastric and duodenal ulcer admitted to the Cook County Hospital. Of these cases 48 were perforated gastric ulcers and 11 perforated duodenal ulcers. During this same period the total number of ulcer cases was 506 gastric ulcers and 72 duodenal ulcers. The frequency of perforation in these cases was 9.4 per cent. in gastric ulcer and 15 per cent. in duodenal ulcer. The patients were seen at varying periods of time after the perforation, some shortly after while others were moribund and in shock. Only those cases in which the perforated ulcer was seen at operation or at autopsy are included in this series. All cases of doubtful diagnosis have been excluded in order to make the data more accurate. Forty-nine of the patients were operated upon by ten different staff surgeons. In the remaining 10 cases the ulcer was recognized at autopsy.

Age and Sex Incidence. Of the perforated gastric ulcers 44 were in males and 4 in females. Caird[1] in a series of 247 cases from the Edinburgh Hospital found a greater percentage of perforated gastric ulcers in females. Connors[2] in a series of 41 cases found 36 in males and 5 in females. The perforated duodenal ulcers were all in males. This agrees with the findings of Caird,[3] who reported 179 males and 21 females in a series of 200 cases.

The majority of the perforations occurred between the ages of thirty and forty years in gastric ulcer and between twenty and thirty years in duodenal ulcer, as will be noted in the following table:

Age.	Gastric ulcer.	Duodenal ulcer.
Under 20 years	1 cases	0 cases
20 to 30 "	12 "	7 "
30 to 40 "	19 "	2 "
40 to 50 "	9 "	2 "
50 to 60 "	4 "	0 "
60 to 70 "	3 "	0 "